REMARKS

The rejection of claims 1 and 3 under 35 U.S.C. § 102(b) as anticipated by Leonhardt *et al.* has been withdrawn. The rejection of claims 1, 3-6, and 11 under 35 U.S.C. § 103(a) as unpatentable over Leonhardt *et al.* in view of U.S. Patent No. 5,919,667 (Gage) has been withdrawn. Claims 1-7, 11, 12 and 15 are currently under examination in the present application. Claims 1-6, 11 and 12 have been rejected and claims 7 and 15 have been objected to. No new matter has been added. Applicants reserve the right to refile this subject matter in a continuation or divisional application filed during the pendency of this application.

Rejection under 35 U.S.C. § 102(b)

Claims 1 and 3 were rejected under 35 U.S.C. § 102 (b) as being anticipated by Licitra *et al.* (1996). The instant claims are drawn to a gene expression modulation system wherein a first gene expression vector comprises a DBD and a LBD; and a second gene expression vector comprises a transactivation domain and LBD not from USP, wherein the LBDs are different. The examiner suggests that these claims are anticipated by Licitra *et al.* because the reference teaches a yeast three-hybrid system comprised of a first gene expression cassette comprising a DNA-binding domain and a ligand binding domain; a second gene expression cassette comprising a different ligand binding domain and a transactivation domain, and a third gene expression cassette comprising a response element and a reporter gene.

Applicants contend that Licitra *et al.* teach a yeast three hybrid hook-bait-fish system in which two ligands, dexamethasone and FK506, that are chemically linked are used to bring two receptors, rat glucocorticoid receptor and human FKBP12 (FK506 binding protein) into close proximity with one another in order to allow for reporter gene activation. The dexamethasone binds to the first receptor, rat glucocorticoid receptor (a nuclear receptor), and the FK506 binds to the second receptor, FKBP12 (an isomerase). Licitra *et al.* do not teach a gene expression system in which the ligand binding domains of the first and second expression cassettes are from nuclear receptors.

Applicants submit that the present invention is an inducible gene expression system which comprises a first expression cassette comprising a DBD and a LBD from a nuclear receptor and a second expression cassette comprising an AD and a LBD

from a nuclear receptor other than USP, wherein the ligand binding domains from the first polypeptide and the second polypeptide are different.

Licitra *et al.* fail to teach or disclose Applicants' invention. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d, 1913, 1920 (Fed. Cir. 1989). The prior art fails to provide each and every element set forth in the present claims for the reasons set forth above.

Thus, Applicants maintain that the cited prior art fails to teach or disclose the present invention as required to set forth anticipation of the claims. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-6, 11 and 12 were rejected under 35 U.S.C. § 103(a) as unpatentable over Licitra *et al.* in view of Gage *et al.* (U.S. Patent No. 5,919,667). The examiner states that the instant claims are drawn to a gene expression modulation system wherein the first gene expression vector comprises a DBD and a LBD; and a second gene expression vector which comprises a transactivation domain and a LBD not from USP. The examiner submits that the Licitra *et al.* reference does not teach LBDs from EcR and RXR. However, the examiner implies that the '667 patent discloses a transgenic animal that contains one or more expression constructs containing nucleic acid encoding an EcR, exogenous RXR and a heterologous gene under the transcription control of an EcR response element, and therefore it would have been obvious to one of skill in the art to make a gene expression modulation system where the first gene expression vector comprises a DBD and an LBD, wherein the LBD is an ecdysone receptor; and a second gene expression vector which comprises a transactivation domain and LBD not from USP.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). For the reasons previously presented above, Applicants

contend that Licitra *et al.* do not teach or suggest all the claim limitations of the present invention, and thus do not support a *prima facie* case of obviousness.

Gage *et al.* teach a MARV vector which can comprise a receptor complex of EcR and RXR, and a MARSHA vector which comprises the gene to be expressed and the response element. Gage *et al.* do not teach the separation of the DBD and AD into the two hybrid format of the present invention. Gage *et al.* do not teach an inducible gene expression system which comprises a first expression cassette comprising a DBD and LBD from a nuclear receptor and a second expression cassette comprising an AD and LBD from a nuclear receptor other than USP. As Licitra *et al.* do not teach the use of LBDs from two different nuclear receptors, which form a heterodimer without the use of bait (2 chemically linked ligands), one of skill in the art would not be motivated to combine these references. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). In the case of Licitra *et al.* there is no use or desirability in modifying the LBDs because the purpose of the study was to construct a yeast three hybrid system using a bait, hook and fish for detecting small ligand-protein receptor interactions, and therefore there is no desirability or motivation to combine those teachings with the teachings of Gage *et al.*

The above combination of prior art fails to suggest Applicants' inventions. The prior art fails to provide the required motivation. There is no suggestion or motivation in any of the cited art itself to make these combinations or to further modify these combinations.

For the reasons set forth above, Applicants maintain that the combination of the cited prior art, when the teachings are taken *as a whole*, fail to supply the motivation required to set forth obviousness of the claims. Accordingly, withdrawal of the rejection is respectfully requested.

Objection

Claims 7 and 15 were objected to as being dependent upon a rejected base claim, but would be allowable if re-written in independent form. Applicants submit that the base claims are in condition for allowance and accordingly request withdrawal of the objection to claims 7 and 15.

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Therefore, Applicants respectfully request reconsideration and withdrawal of all of the above rejections.

Respectfully submitted,

Camille Jolly-Tornetta

Camille Jolly-Tornetta, Ph.D.
Registration No. 48,592

RheoGene, Inc.
2650 Eisenhower Avenue
Norristown, PA 19403
Telephone: (610) 650-8734
Fax: (610) 650-8755

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